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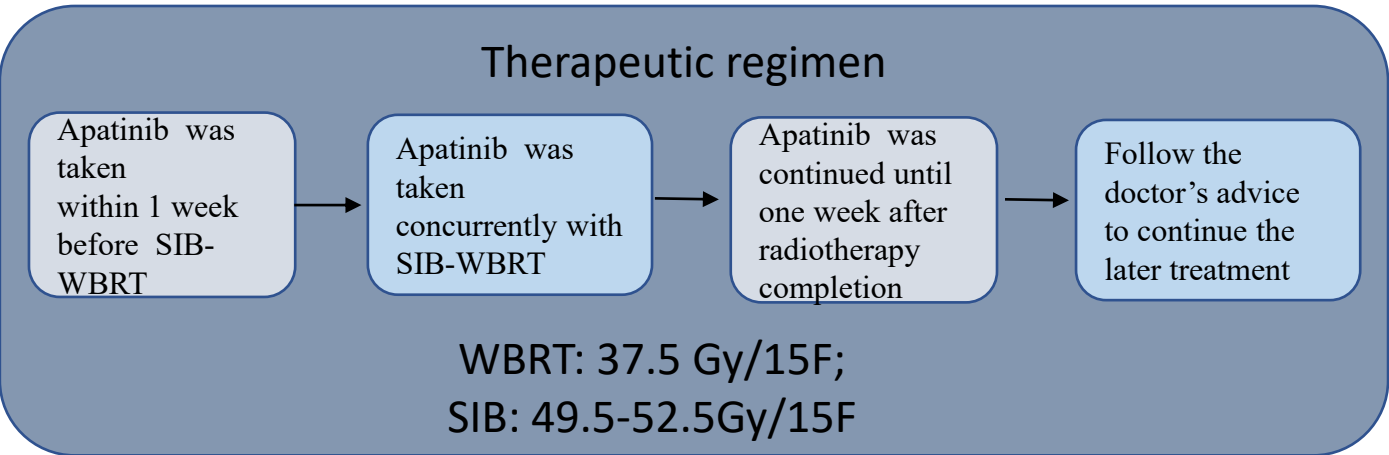
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BACKGROUND

Brain metastases (BM) develop during the disease course in 20-65% of lung cancer patients. Neo-angiogenesis is crucial to the growth of brain metastases (BM); anti-angiogenic therapy could offer additional benefits including radiosensitization. This prospective pilot study explored the safety and efficacy of whole brain radiotherapy with simultaneous integrated boost (SIB-WBRT) and concurrent apatinib.

METHODS

This trial enrolled 16 patients with non-recurrent BM from histologically confirmed NSCLC.

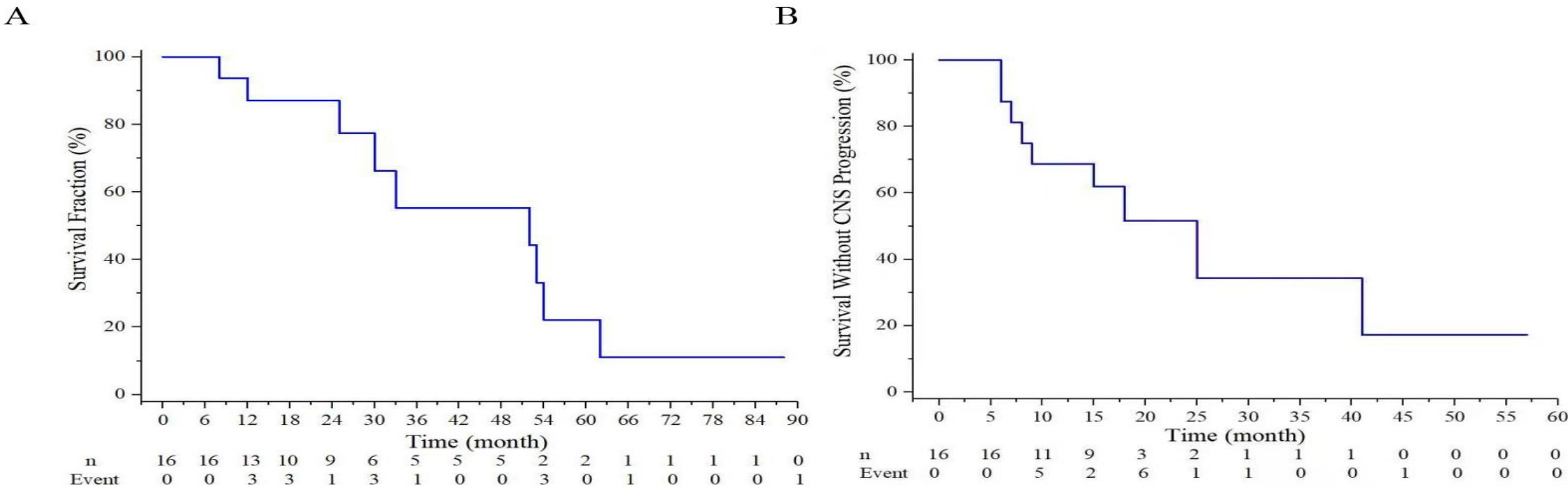


iORR, iDCR, iPFS, OS, and safety was calculated and evaluated.

iORR: intracranial objective response rate; iDCR: intracranial disease control rate; iPFS: intracranial progression-free survival; OS: overall survival

The toxicity was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) V4.0. Each follow-up MRI was evaluated for disease response based on the Response Evaluation Criteria in Solid Tumors (RECIST V1.1).

RESULTS: Efficacy



Outcomes of the trial population

Outcome	time (months)	(%)
Median overall time, months	26	
6-month rate		100
1-year rate		87.5
2-year rate		56.3
CNS progression-free survival median time, months	16.5	
6-month rate		100
1-year rate		68.8
2-year rate		18.8

BM responses of the trial population

BM RECIST response	No.	%
CR	1	6.25
PR	11	68.75
SD	4	25
PD	0	0

- At 3-6 months following SIB-WBRT, 1 patient achieved the intracranial complete response (CR), 11 patients got the partial response (PR), 4 patients reached the stable disease (SD) and no patient was found progression disease (PD). Therefore, iORR was 75% and iDCR was 100%.
- The median iPFS was 16.5 months (95% confidence interval (CI), 15.1-37.4 months), and the median OS was 26 months (95% CI, 31.6-58.1 months).

Baseline Characteristics

This trial (July 2016 to March 2020) analyzed 16 patients (10 males and 6 females) and their median age was 58 years old. Fourteen patients were adenocarcinoma and 14 patients had a Karnofsky performance status of 80-90; 10 (62.5%) had 1-3 BM. Four patients with EGFR mutations: three with exon 19 deletions and one with exon 21 L858R mutation. The median diagnosis-specific Graded Prognostic Assessment (GPA) score was 2.5.

RESULTS: Safety

Nine patients initially received 500 mg apatinib, of whom two patients experienced grade 3 events (hypertension and oral mucositis) and required a dose reduction to 250 mg. Aside from these patients, there were no other grade 3-5 toxicities. Grade 2 events were also limited, including two cases of hand-foot syndrome and one case each of oral mucositis, hypertension, fatigue, hoarseness, anorexia, and hyperbilirubinemia.

CONCLUSION

This prospective trial of concurrent apatinib and SIB-WBRT for NSCLC BM yielded excellent tolerance as well as encouraging outcomes.